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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
10/546,132	12/12/2005	Rulin Fan	EISN-009USRCE	9915
78844	7590	09/09/2008	EXAMINER	
Lahive & Cockfield, LLP/EISAI			OLSON, ERIC	
Floor 30, Suite 3000				
One Post Office Square			ART UNIT	PAPER NUMBER
Boston, MA 02109			1623	
			MAIL DATE	DELIVERY MODE
			09/09/2008	PAPER

**Please find below and/or attached an Office communication concerning this application or proceeding.**

The time period for reply, if any, is set in the attached communication.

<b>Office Action Summary</b>	<b>Application No.</b> 10/546,132	<b>Applicant(s)</b> FAN, RULIN	
	<b>Examiner</b> Eric S. Olson	<b>Art Unit</b> 1623	

**-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --**

**Period for Reply**

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

**Status**

- 1) ☒ Responsive to communication(s) filed on 02 July 2008.
- 2a) ☐ This action is **FINAL**.                      2b) ☒ This action is non-final.
- 3) ☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

**Disposition of Claims**

- 4) ☒ Claim(s) 120-123, 125, 126, 128, 130-133, 135, 136 and 138 is/are pending in the application.
- 4a) Of the above claim(s) \_\_\_\_\_ is/are withdrawn from consideration.
- 5) ☐ Claim(s) \_\_\_\_\_ is/are allowed.
- 6) ☒ Claim(s) 120-123, 125, 126, 128, 130-133, 135, 136 and 138 is/are rejected.
- 7) ☐ Claim(s) \_\_\_\_\_ is/are objected to.
- 8) ☐ Claim(s) \_\_\_\_\_ are subject to restriction and/or election requirement.

**Application Papers**

- 9) ☐ The specification is objected to by the Examiner.
- 10) ☐ The drawing(s) filed on \_\_\_\_\_ is/are: a) ☐ accepted or b) ☐ objected to by the Examiner.  
Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).  
Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).
- 11) ☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

**Priority under 35 U.S.C. § 119**

- 12) ☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).
- a) ☐ All    b) ☐ Some \*    c) ☐ None of:
1. ☐ Certified copies of the priority documents have been received.
2. ☐ Certified copies of the priority documents have been received in Application No. \_\_\_\_\_.
3. ☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

\* See the attached detailed Office action for a list of the certified copies not received.

**Attachment(s)**

- |  |   |
|--|---|
| 1) <input checked="" type="checkbox"/> Notice of References Cited (PTO-892)          | 4) <input type="checkbox"/> Interview Summary (PTO-413)           |
| 2) <input type="checkbox"/> Notice of Draftsperson's Patent Drawing Review (PTO-948) | Paper No(s)/Mail Date. _____                                      |
| 3) <input type="checkbox"/> Information Disclosure Statement(s) (PTO/SB/08)          | 5) <input type="checkbox"/> Notice of Informal Patent Application |
| Paper No(s)/Mail Date _____  | 6) <input type="checkbox"/> Other: _____                          |

### **Detailed Action**

A request for continued examination under 37 CFR 1.114, including the fee set forth in 37 CFR 1.17(e), was filed in this application after final rejection. Since this application is eligible for continued examination under 37 CFR 1.114, and the fee set forth in 37 CFR 1.17(e) has been timely paid, the finality of the previous Office action has been withdrawn pursuant to 37 CFR 1.114. Applicant's submission filed on July 2, 2008 has been entered.

This office action is a response to applicant's communication submitted July 2, 2008 wherein claims 127 and 137 are cancelled. This application is a national stage application of PCT/US04/04921, filed February 18, 2004, which claims benefit of provisional application 60/448839, filed February 20, 2003.

Claims 120-123, 125, 126, 128, 130-133, 135, 136, and 138 are pending in this application.

Claims 120-123, 125, 126, 128, 130-133, 135, 136, and 138 as amended are examined on the merits herein.

The declaration under 37 CFR 1.132 by James E. Foy filed July 2, 2008 has been fully considered and entered into the record. This declaration is discussed further below as it relates to the rejections of record in this office action.

Applicant's arguments, submitted July 2, 2008, with respect to the rejection of instant claims 120-123, 125-128, 130-133, and 135-138 under 35 USC 103(a) for being

Art Unit: 1623

obvious over Rossignol et al., has been fully considered and found to be persuasive to remove the rejection as Rossignol et al. gives no guidance as to how to successfully carry out a synthesis using the claimed intermediates in view of the difficulties encountered with the use of oxone® or phosgene. Therefore the rejection is withdrawn.

The following new grounds of rejection are introduced:

***Claim Rejections - 35 USC § 103***

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

(a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negated by the manner in which the invention was made.

Claims 120-123 and 130-133 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossignol et al. (US patent 6184366, of record in previous action) in view of Sanghvi et al. (US patent 6809195, cited in PTO-892)

Rossignol et al. discloses the synthesis of lipopolysaccharides of which the claimed compounds are substructures. (columns 3 and 4, top of page) Specifically, a synthesis is disclosed in which two lipomonosaccharide components, corresponding to the left and right halves of the lipopolysaccharide, are synthesized and then joined together. (columns 13-14) The left half bears a close structural resemblance to the compounds of claims 120-123 and 130-133. Columns 34-36 and 46 disclose synthetic intermediates that are the same as those claimed in instant claims 120-123 and 130-133, except that they have a NHTroc protecting group in place of the fatty acid amide

moiety. Rossignol et al. does not disclose the specific claimed compounds. However, if the order of the synthetic steps performed by Rossignol et al. were changed so that the fatty amide group were attached first before the other synthetic steps, the resulting intermediates would be identical to the compounds of claims 120-123 and 130-133.

Sanghvi et al. discloses a process for preparing oligonucleotides. (column 4 lines 10-35) One step in the synthesis involves the oxidation of a phosphite group to a phosphate. (column 5 lines 45-50) Oxidizing reagents suitable for carrying out this step include a wide range of different reagents which are not oxone®. (column 5 line 64 - column 6 line 8)

It would have been obvious to one of ordinary skill in the art at the time of the invention to carry out the synthesis described by Rossignol et al. using a different order of synthetic steps that would result in the claimed intermediates, using any of the methods described by Sanghvi et al. to oxidize the phosphorus atom to phosphate. One of ordinary skill in the art would have been motivated to carry out this synthesis because Rossignol et al. already teaches all of the individual steps involved in synthesizing this saccharide. Adding the functional groups in one order or another would be well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Arguments: Applicant's arguments, submitted July 2, 2008, have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that one of ordinary skill in the art would not be able to carry out the synthesis in a different order because the alkene group in the fatty acid moiety would not be

Art Unit: 1623

compatible with the use of the oxone® reagent to oxidize the phosphorus atom, as described by Bloch et al. Firstly, the compounds of claims 121-123 and 131-133 already have the protected phosphate group attached. If the fatty acid amide were introduced immediately after the introduction and oxidation of the phosphate group the resulting intermediates would be these compounds, without subjecting the alkene moiety to oxone®, as described in figures 1 and 2 below.

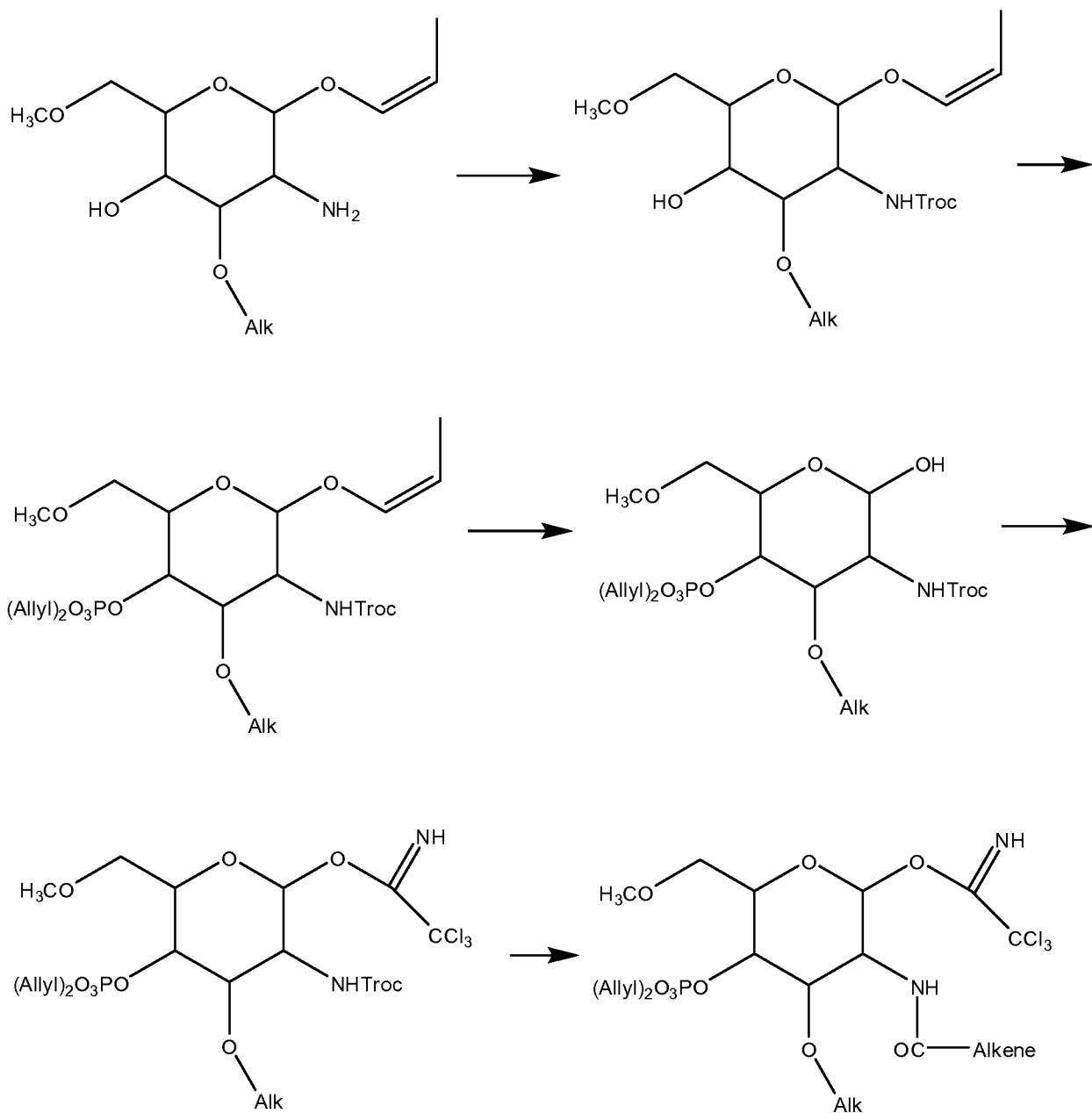


Figure 1 - Synthesis as described in '366

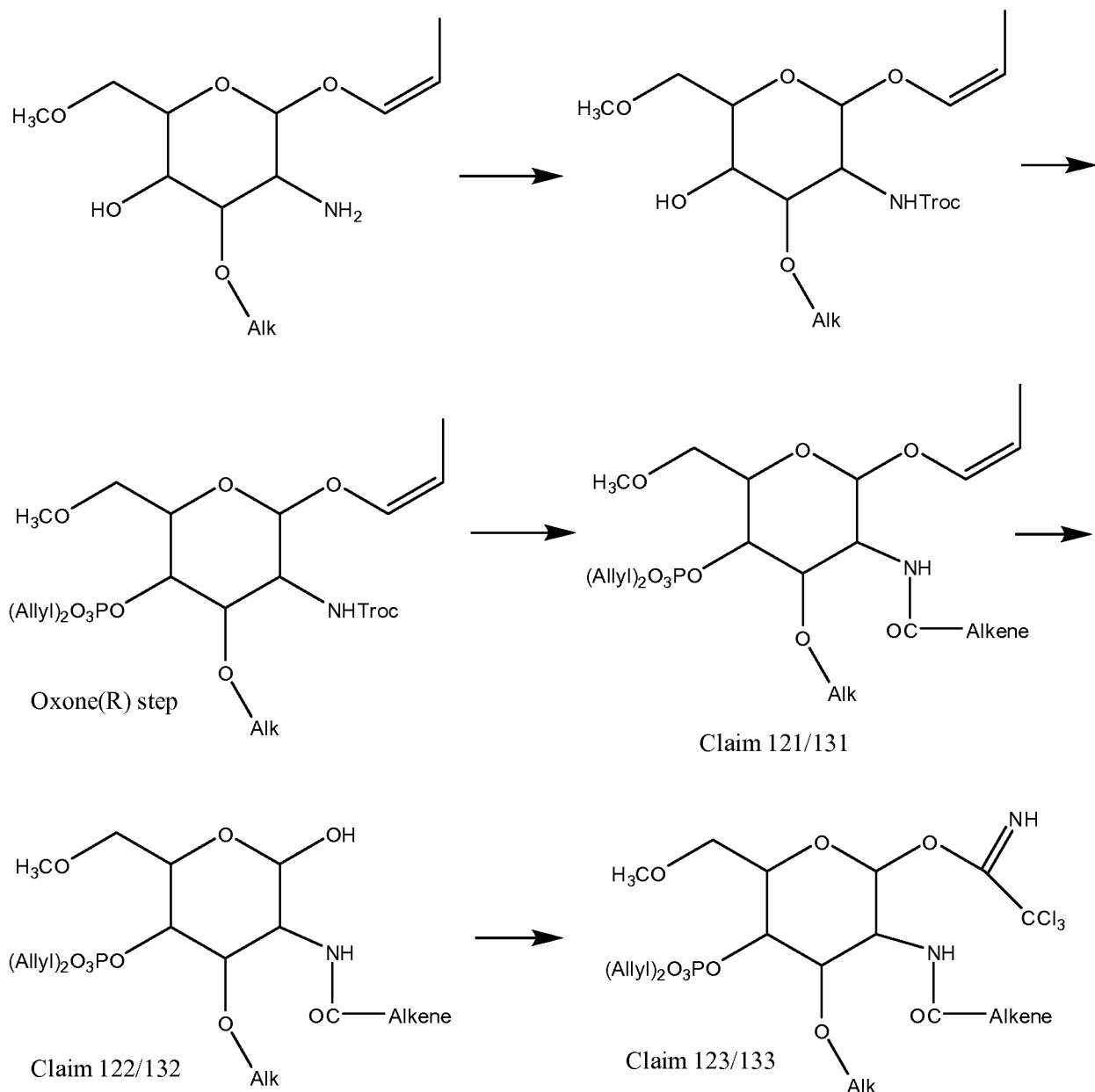


Figure 2 - Synthesis in different order as described in the rejection

Furthermore, Sanghvi et al. discloses a number of different oxidants that can be used to oxidize a phosphorus(III) atom to phosphate. One of ordinary skill in the art would thus be able to substitute other reagents for persulfate and avoid the



Art Unit: 1623

incompatible combination described by Bloch et al., thus being able to carry out the synthetic process in which the fatty amide is introduced before the introduction of phosphate.

The Foy declaration has been fully considered but is not persuasive to remove the rejection as it concerns only one specific method of oxidizing phosphorus. One of ordinary skill in the art would have been able to substitute a different method that would be compatible with the presence of an alkene. Therefore it is not surprising that one of ordinary skill in the art could have practiced a synthetic scheme using these compounds as intermediates.

For these reasons the rejection is deemed proper and maintained.

Claims 125, 126, 128, 135, 136, and 138 are rejected under 35 U.S.C. 103(a) as being unpatentable over Rossignol et al. (US patent 6184366, of record in previous action) in view of Greene et al. (Reference of record with PTO-892)

Rossignol et al. discloses the synthesis of lipopolysaccharides of which the claimed compounds are substructures. (columns 3 and 4, top of page) Specifically, a synthesis is disclosed in which two lipomonosaccharide components, corresponding to the left and right halves of the lipopolysaccharide, are synthesized and then joined together. (columns 13-14) The right half bears a close structural resemblance to the compounds of claims 125, 126, 128, 135, 136, and 138. Columns 37-44 disclose synthetic intermediates that are the same as those claimed in instant claims 125, 126, 128, 135, 136, and 138, except that they have a diphenyl ketone imine protecting group

Art Unit: 1623

in place of the fatty acid amide moiety. Rossignol et al. does not disclose the specific claimed compounds. However, if the order of the synthetic steps performed by Rossignol et al. were changed so that the fatty amide group were attached first before the other synthetic steps, the resulting intermediates would be identical to the compounds of claims 125, 126, 128, 135, 136, and 138.

Greene et al. discloses various methods of introducing an allyl carbonate protecting group. (pp. 183-184) These methods do not involve using phosgene.

It would have been obvious to one of ordinary skill in the art at the time of the invention to carry out the synthesis described by Rossignol et al. using a different order of synthetic steps that would result in the claimed intermediates, using any of the methods described by Greene et al. to introduce the allyl carbonate group. One of ordinary skill in the art would have been motivated to carry out this synthesis because Rossignol et al. already teaches all of the individual steps involved in synthesizing this saccharide. Adding the functional groups in one order or another would be well within the ordinary and routine level of skill in the art.

Therefore the invention taken as a whole is *prima facie* obvious.

Response to Arguments: Applicant's arguments, submitted July 2, 2008, have been fully considered and not found to be persuasive to remove the rejection. Applicant argues that one of ordinary skill in the art would not be able to carry out the synthesis in a different order because the amide group in the fatty acid moiety would not be compatible with the use of phosgene to introduce allyl carbonate, as described by US patent 3282923. However, as described by Greene et al., one of ordinary skill in the art

Art Unit: 1623

could have used various different methods for introducing an allyl carbonate, which do not require using phosgene. Selecting a known protecting group introducing step from those already well known in the art (as exemplified by a reference book such as Greene et al.) for compatibility with the functional groups present in a target molecule is well within the ordinary and routine level of skill in the art.

The Foy declaration has been fully considered but is not persuasive to remove the rejection as it concerns only one specific method of oxidizing phosphorus. One of ordinary skill in the art would have been able to substitute a different method that would be compatible with the presence of an amide. Therefore it is not surprising that one of ordinary skill in the art could have practiced a synthetic scheme using these compounds as intermediates.

For these reasons the rejection is deemed proper and maintained.

### **Conclusion**

No claims are allowed in this application.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Eric S. Olson whose telephone number is 571-272-9051. The examiner can normally be reached on Monday-Friday, 8:30-5:00.

If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Shaojia Anna Jiang can be reached on (571)272-0627. The fax phone number for the organization where this application or proceeding is assigned is 571-273-8300.

Art Unit: 1623

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see <http://pair-direct.uspto.gov>. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free). If you would like assistance from a USPTO Customer Service Representative or access to the automated information system, call 800-786-9199 (IN USA OR CANADA) or 571-272-1000.

/Eric S Olson/  
Examiner, Art Unit 1623  
9/4/2008

/Shaojia Anna Jiang, Ph.D./  
Supervisory Patent Examiner, Art Unit 1623